Translation

PCT/JP2004/005316

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference KW0122	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2004/005316	International filing date (*day/month/year*) 14 April 2004 (14.04.2004)	Priority date (*day/month/year*) 17 April 2003 (17.04.2003)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 31/366, 31/404, 31/4418, 31/40, 31/505, 31/47, 31/22, A61P 9/00, 9/10, C12N 15/00		
Applicant KOWA CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) disk 1 _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18 October 2004 (18.10.2004)	28 February 2005 (28.02.2005)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/005316

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP04/005316

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 17-24

because:

☒ the said international application, or the said claims Nos. 17-24 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject matters of claims 17-24 encompass a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with the provisions of PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 17-24 .

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims		YES
	Claims	1-16	NO
Inventive step (IS)	Claims		YES
	Claims	1-16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Effects of Statins on Vascular Wall: Vasomotor Function, Inflammation, and Plaque Stability, (K.K. Koh), Cardiovasc. Res., 2000, Vol. 47, No. 4, pages 648-657
Document 2: WO, 2002-030425, A1 (Nissan Chemical Industries, Ltd.), 18 April, 2002 (18.04.02)

Document 1 cited in the ISR describes that statins are useful for treatment of vascular diseases and that their effect is associated with the mevalonate pathway because it is inhibited by addition of mevalonic acid, etc., (see Abstract, page 654, Conclusion, etc.).

Document 2 cited in the ISR describes a treatment agent for complications of diabetes having statins, particularly pitavastatin, as an active ingredient (see claim 4), and suggests that pitavastatin's effect of inhibiting the production of mevalonic acid is associated with the treatment (see page 12, line 7 to the last line).

Claims 1-16

The above claims of the present application relate to the invention of agents promoting the expression of LKLF/KLF2 gene that have substances to inhibit the mevalonate metabolic pathway as an active ingredient; on the other hand, documents 1 and 2 do not describe the promotion of expression of LKLF/KLF2 gene.

However, it is recognized that the agents promoting the expression of LKLF/KLF2 gene in the above claims of the present application encompass medicinal agents for treatment of vascular diseases such as diabetes (see page 1 in the specification of the present application). The subject matters of the above claims of the present application are thus the same as the inventions described in documents 1 and 2 in respect of both the active ingredients and the applied diseases, and so the former as such substances are indistinguishable from the latter as such substances.

Accordingly, the subject matters of claims 1-16 of the present application do not appear to be novel or to involve an inventive step in view of documents 1 and 2.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1, 6, 7, 9, 14 and 15

The above claims of the present application describe compounds defined in terms of desired properties such as "substances to block the mevalonate metabolic pathway", "agents to inhibit farnesyl transferase", and "agents to inhibit geranylgeranyl transferase I". The above claims thus encompass all the cases of use of the compounds having such properties; however, only a small portion of the claimed compounds is disclosed in the sense of PCT Article 5, and the above claims are not supported by the disclosure in the sense of PCT Article 6 in the specification.

For the "substances to block the mevalonate metabolic pathway", the "agents to inhibit farnesyl transferase", or the "agents to inhibit geranylgeranyl transferase I", the scope of compounds that have such property cannot be specified, even based on the common technical knowledge at the time of filing of the present application. Accordingly, the above claims do not satisfy the requirement of clearness according to PCT Article 6.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*